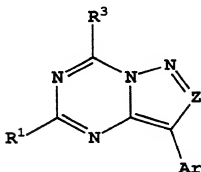


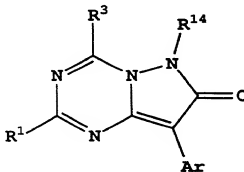
CLAIMS

WHAT IS CLAIMED IS:

- 5 1. A method of treating affective disorder,
 anxiety, depression, headache, irritable bowel
 syndrome, post-traumatic stress disorder, supranuclear
 palsy, immune suppression, Alzheimer's disease,
 gastrointestinal diseases, anorexia nervosa or other
 10 feeding disorder, drug addiction, drug or alcohol
 withdrawal symptoms, inflammatory diseases,
 cardiovascular or heart-related diseases, fertility
 problems, human immunodeficiency virus infections,
 hemorrhagic stress, obesity, infertility, head and
 15 spinal cord traumas, epilepsy, stroke, ulcers,
 amyotrophic lateral sclerosis, hypoglycemia or a
 disorder the treatment of which can be effected or
 facilitated by antagonizing CRF, including but not
 limited to disorders induced or facilitated by CRF, in
 20 mammals comprising administering to the mammal a
 therapeutically effective amount of a compound of
 Formulae (1) or (2):



(1)



(2)

25

and isomers thereof, stereoisomeric forms thereof, or
 mixtures of stereoisomeric forms thereof, and

pharmaceutically acceptable salt forms thereof,
wherein:

Z is N or CR²;

5

Ar is selected from phenyl, naphthyl, pyridyl,
pyrimidinyl, triazinyl, furanyl, thienyl,
benzothienyl, benzofuranyl, 2,3-
dihydrobenzofuranyl, 2,3-dihydrobenzothienyl,
10 indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-
benzopyranyl, tetralinyl, each Ar optionally
substituted with 1 to 5 R⁴ groups and each Ar is
attached to an unsaturated carbon atom;

15 R¹ is independently selected at each occurrence from
H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-
20 C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;

R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-
C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -
25 NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-
C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;

R³ is selected from:

-H, OR⁷, SH, S(O)_nR¹³, COR⁷, CO₂R⁷,
30 OC(O)R¹³, NR⁸COR⁷, N(COR⁷)₂, NR⁸CONR⁶R⁷,
NR⁸CO₂R¹³, NR⁶R⁷, NR⁶Ar^{7a}, N(OR⁷)R⁶,
CONR⁶R⁷, aryl, heteroaryl and heterocyclyl,
or
-C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
35 C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₄-
C₁₂ cycloalkylalkyl or C₆-C₁₀

- cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl and heterocyclyl;
- 10 R⁴ is independently selected at each occurrence from:
 C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂, halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷,
 15 NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷, or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl and C₄-C₁₂ cycloalkylalkyl are optionally substituted with 1 to 3 substituents
 20 independently selected at each occurrence from C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷, NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷, or S(O)_nR⁷;
- 25 R⁶, R⁷, R^{6a} and R^{7a} are independently selected at each occurrence from:
 -H,
 -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
 30 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each
 35 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,

- cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 heteroaryl or heterocyclyl,
 5 -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 heterocyclyl(C₁-C₄ alkyl);
- alternatively, NR^{6R7} and NR^{6aR7a} are independently
 10 piperidine, pyrrolidine, piperazine, N-
 methylpiperazine, morpholine or thiomorpholine, each
 optionally substituted with 1-3 C₁-C₄ alkyl groups;
- 15 R⁸ is independently selected at each occurrence from H
 or C₁-C₄ alkyl;
- R⁹ and R¹⁰ are independently selected at each
 occurrence from H, C₁-C₄ alkyl, or C₃-C₆
 cycloalkyl;
 20 R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl,
 or C₃-C₆ cycloalkyl;
- R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl;
 25 R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-
 C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-,
 heteroaryl or heteroaryl(C₁-C₄ alkyl)-;
 30 R¹⁴ is selected from C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-
 C₁₀ alkynyl, C₃-C₈ cycloalkyl, or C₄-
 C₁₂ cycloalkylalkyl, each optionally substituted
 with 1 to 3 substituents independently selected
 35 at each occurrence from C₁-C₆ alkyl, C₃-

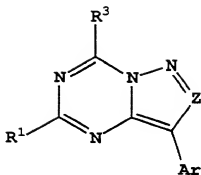
5 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, and C₁-C₆ alkylthio, C₁-C₆ alkylsulfinyl and C₁-C₆ alkylsulfonyl;

10 R¹⁵ and R¹⁶ are independently selected at each occurrence from H, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that for S(O)_nR¹⁵, R¹⁵ cannot be H;

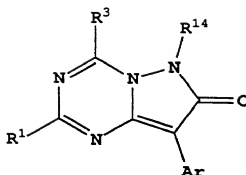
15 aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

20 heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranal, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, 25 benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, 30 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

- heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
- 5 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and CONR¹⁶R¹⁵;
- 10 n is independently at each occurrence 0, 1 or 2;
- with the proviso that when Z is CR², then R³ is not NR⁶R⁷, NR^{6a}R^{7a} or OR⁷.
- 15 2. A method of claim 1 wherein, in the compound of Formulae (1) or (2), Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, each optionally substituted with 1 to 4 R⁴ substituents.
- 20 3. A method of claim 1 wherein, in the compound of Formulae (1) or (2), A is N, Z is CR², Ar is 2,4-dichlorophenyl, 2,4-dimethylphenyl or 2,4,6-trimethylphenyl, R¹ and R² are CH₃, and R³ is NR^{6a}R^{7a}.
- 25 4. A compound of Formulae (1) or (2):



(1)



(2)

and isomers thereof, stereoisomeric forms thereof, or
 5 mixtures of stereoisomeric forms thereof, and
 pharmaceutically acceptable salt forms thereof
 wherein:

Z is N or CR²;

10

Ar is selected from phenyl, naphthyl, pyridyl,
 pyrimidinyl, triazinyl, furanyl, thienyl,
 benzothienyl, benzofuranyl, 2,3-
 dihydrobenzofuranyl, 2,3-dihydrobenzothienyl,
 15 indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-
 benzopyranyl, tetralinyl, each Ar optionally
 substituted with 1 to 5 R⁴ groups and each Ar is
 attached to an unsaturated carbon atom;

20

R¹ is independently selected at each occurrence from
 H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
 halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
 C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
 cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-
 25 C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;

R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;

R³ is selected from:
 -H, OR⁷, SH, S(O)_nR¹³, COR⁷, CO₂R⁷,
 OC(O)R¹³, NR⁸COR⁷, N(COR⁷)₂, NR⁸CONR⁶R⁷,
 NR⁸CO₂R¹³, NR⁶R⁷, NR^{6a}R^{7a}, N(OR⁷)R⁶,
 CONR⁶R⁷, aryl, heteroaryl and heterocyclyl,
 or
 -C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
 C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₄-C₁₂ cycloalkylalkyl or C₆-C₁₀
 cycloalkenylalkyl, each optionally
 substituted with 1 to 3 substituents
 independently selected at each occurrence
 from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo,
 C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
 S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³,
 NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 heteroaryl and heterocyclyl;

R⁴ is independently selected at each occurrence from:
 C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
 C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂,
 halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷,
 NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷,
 or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl and C₄-C₁₂ cycloalkylalkyl are optionally substituted with 1 to 3 substituents
 independently selected at each occurrence from

C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷,
 NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷,
 or S(O)_nR⁷;

- 5 R⁶, R⁷, R^{6a} and R^{7a} are independently selected at each occurrence from:

-H,

- C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
 10 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
 or C₆-C₁₄ cycloalkenylalkyl, each
 optionally substituted with 1 to 3
 substituents independently selected at each
 15 occurrence from C₁-C₆ alkyl, C₃-
 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 20 heteroaryl or heterocyclyl,
 -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 heterocyclyl(C₁-C₄ alkyl),

alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently

- 25 piperidine, pyrrolidine, piperazine, N-
 methylpiperazine, morpholine or thiomorpholine, each
 optionally substituted with 1-3 C₁-C₄ alkyl groups;

- R⁸ is independently selected at each occurrence from H
 30 or C₁-C₄ alkyl;

R⁹ and R¹⁰ are independently selected at each
 occurrence from H, C₁-C₄ alkyl, or C₃-C₆
 cycloalkyl;

35

R11 is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl,
or C₃-C₆ cycloalkyl;

R12 is C₁-C₄ alkyl or C₁-C₄ haloalkyl;

5

R13 is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-
C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-,
heteroaryl or heteroaryl(C₁-C₄ alkyl)-;

10

R14 is selected from C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-
C₁₀ alkynyl, C₃-C₈ cycloalkyl, or C₄-
C₁₂ cycloalkylalkyl, each optionally substituted

15

with 1 to 3 substituents independently selected
at each occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano,
OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵,
NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵,
NR¹⁶R¹⁵, CONR¹⁶R¹⁵, and C₁-C₆ alkylthio, C₁-C₆

20

alkylsulfinyl and C₁-C₆ alkylsulfonyl;

R15 and R16 are independently selected at each
occurrence from H, C₁-C₆ alkyl, C₃-C₁₀
cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that
for S(O)_nR¹⁵, R¹⁵ cannot be H;

25

aryl is phenyl or naphthyl, each optionally
substituted with 1 to 5 substituents
independently selected at

30

each occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano,
OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵,
NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵,
NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

35

heteroaryl is pyridyl, pyrimidinyl, triazinyl,
 furanyl, pyranyl, quinolinyl, isoquinolinyl,
 thienyl, imidazolyl, thiazolyl, indolyl,
 pyrrolyl, oxazolyl, benzofuranyl, benzothienyl,
 5 benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-
 dihydrobenzothienyl or 2,3-dihydrobenzofuranyl,
 each being optionally substituted with 1 to 5
 substituents independently selected at each
 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
 10 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
 S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵,
 N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and
 CONR¹⁶R¹⁵;

15 heterocyclyl is saturated or partially saturated
 heteroaryl, optionally substituted with 1 to 5
 substituents independently selected at each
 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
 20 S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵,
 N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and
 CONR¹⁶R¹⁵;

n is independently at each occurrence 0, 1 or 2;

25 with the provisos that:

- 30 (1) when Z is CR² and R² is H and R³ is OCOR¹³ and
 R⁷ is H, then R¹ is not H, OH or SH;
- (2) when Z is CR² and R¹ is CH₃ or C₂H₅ and R² is H,
 and R³ is H, CH₃, C₂H₅, C₆H₅, n-C₃H₇, i-C₃H₇, SH or
 SCH₃, then Ar is not phenyl or m-CH₃-phenyl;
- 35 (3) when Z is CR² and R² is -NR⁶SO₂R⁷ or -SO₂NR⁶R⁷,
 then R³ is not SH; and

(4) when Z is CR², then R³ is not NR⁶R⁷, NR^{6a}R^{7a} or OR⁷.

- 5 5. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, each optionally
- 10 substituted with 1 to 4 R⁴ substituents.
6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 4.
- 15 7. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 5.
- 20 8. A compound of Formula (2) of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof.
- 25 9. A compound of claim 8 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl and each Ar is
- 30 optionally substituted with 1 to 4 R⁴ substituents.
10. A compound of claim 8 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically
- 35 acceptable salt forms thereof wherein R³ is NR^{6a}R^{7a} or OR⁷.

11. A compound of claim 8 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents, and R³ is NR^{6a}R^{7a} or OR⁷.
12. A compound of Formula (1) of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Z is CR².
13. A compound of claim 12 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl and each Ar is optionally substituted with 1 to 4 R⁴ substituents.
14. A compound of claim 19 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

R^{6a} is independently selected from:

- H,
- C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
- C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-

- C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
- 5 heteroaryl or heterocyclyl, -aryl, aryl(C₁-C₄ alkyl)-, heteroaryl, heteroaryl(C₁-C₄ alkyl)-, heterocyclyl or heterocyclyl(C₁-C₄ alkyl)-; and
- R^{7a} is independently selected at each occurrence from:
- 10 -H,
-C₅-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
- 15 or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
- 20 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl, -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
- 25 heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl);

- alternatively, NR^{6R7} and NR^{6aR7a} are independently piperidine, pyrrolidine, piperazine, N-
- 30 methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C₁-C₄ alkyl groups.

15. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

- R^{6a} and R^{7a} are identical and are selected from:
- 5 -C₁-C₄ alkyl or C₃-C₆ cycloalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, -COR¹⁵,
 - 10 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl, and -aryl or heteroaryl.
 - 15 16. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:
 - 20 R^{6a} is selected from:
 - H,
 - C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 - 25 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-
 - 30 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl,

-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl);

R^{7a} is selected from:

- 5 -C₁-C₄ alkyl and each such C₁-C₄ alkyl is
substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)NR¹³, COR¹⁵,
10 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl.

17. A compound of claim 4 and isomers thereof,
15 stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein:

- one of R^{6a} and R^{7a} is selected from:
20 -C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
optionally substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)NR¹³, COR¹⁵,
25 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl,
-aryl,
-heteroaryl or
30 -heterocyclyl,
and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄
alkyl.

18. A compound of claim 4 and isomers thereof,
35 stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl, each such C₁-C₁₀ alkyl optionally substituted with

5 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,

10 heteroaryl or heterocyclyl.

19. A compound of claim 14 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically

15 acceptable salt forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents.

20. A compound of claim 15 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is

20 optionally substituted with 1 to 4 R⁴ substituents.

25 21. A compound of claim 16 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl,

30 pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents.

22. A compound of claim 17 and isomers thereof, stereoisomeric forms thereof, or mixtures of

35 stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein Ar is phenyl,

pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents.

23. A compound of claim 18 and isomers thereof,
5 stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein Ar is phenyl,
pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is
optionally substituted with 1 to 4 R⁴ substituents.

10

24. A compound of claim 4 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein

15 -Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents,
-R¹ and R² are independently selected from H, C₁-C₄
alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
20 cycloalkylalkyl.

20

25. A compound of claim 14 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically

25 acceptable salt forms thereof wherein

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents,
-R¹ and R² are independently selected from H, C₁-C₄
30 alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl.

30

26. A compound of claim 15 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
35 stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents,

- 5 -R¹ and R² are independently selected from H, C₁-C₄
alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl.

27. A compound of claim 16 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
10 stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein

- Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents,
15 -R¹ and R² are independently selected from H, C₁-C₄
alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl.

28. A compound of claim 17 and isomers thereof,
20 stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein

- Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents,
25 -R¹ and R² are independently selected from H, C₁-C₄
alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl.

- 30 29. A compound of claim 18 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein

- Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
35 and each Ar is optionally substituted with 1
to 4 R⁴ substituents,

-R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

- 5 30. A compound of claim 24 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl,
- 10 each such C₁-C₁₀ alkyl optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
- 15 R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

31. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R¹ is independently selected at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl, C₂-C₁₂ alkoxyalkyl,
- 20 C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.
- 25

32. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -NR⁶R⁷, C₁-C₄ haloalkyl, -OR⁷.
- 30

33. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R^4 is independently selected at each occurrence from: C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, COR⁷, OR⁷, where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₃-C₆ cycloalkyl and C₄-C₁₂ cycloalkylalkyl are optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₄ alkyl, NR⁶R⁷, COR⁷ OR⁷, CO₂R⁷.
34. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R^4 is independently selected at each occurrence from: H, C₁-C₁₀ alkyl, C₁-C₄ alkoxy, halo, CN and -NR⁶R⁷.
35. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 5, 14, 15 and 19.
36. A method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis,

hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals comprising administering to the mammal a therapeutically effective amount of a compound of claim 4, 5, 14, 15 and 19.

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